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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/785,951	02/16/2001	Michael John Mullan	01097.0008U2	7348

7590 06/13/2002

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EXAMINER
CROUCH, DEBORAH

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/13/2002

07

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/785,951	MULLAN, MICHAEL JOHN	
	Examin r	Art Unit	
	Deborah Crouch	1632	

-- The MAILING DATE of this communication app ars on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

This is continuation of 09/058,384, abandoned.

Applicant has compiled with the sequence rules.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 25 and 27 are rejected under 35 U.S.C. 101 because they are drawn to non-statutory subject matter. "Host" is viewed as encompassing humans, and thus encompasses non-statutory subject matter. It is PTO policy not to allow claims to humans or claims that encompass humans (see 1077 OG 24, April 21. 1987). This rejection can be overcome by inserting "non-human" before "animal". However, it seems that a less restrictive amendment would be to state an isolated cell. This covers applicants disclosure of prokaryotic and eukaryotic cells transformed with nucleic acid sequence encoding human amyloid precursor protein APP 770, wherein the amino acid encodes at amino acid 670 other than lysine and/or at amino acid 671 other than methionine, and further encodes other than valine at amino acid 717.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 25-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 12 of U.S. Patent No. 5,455,169. Although the conflicting claims are not identical, they are not patentably distinct from each other because the specific nucleic acid sequences claimed in claims 11 and 12 of '169 are encompassed within the scope of claims 25-28 in the instant claims. Further, the instant specification defines a nucleic acid sequence encoding human amyloid precursor protein APP 770, wherein the amino acid encodes at amino acid 670 other than lysine and/or at amino acid 671 other than methionine, and further encodes other than valine at amino acid 717 as encompassing the specific sequences claimed in claims 11 and 12 of '169, and also defines host as "an immortalized mammalian cell line". Thus, given claims 11 and 12 of '169, it would have been obvious at the time of the instant invention to make a host containing a nucleic acid sequence encoding human amyloid precursor protein APP 770, wherein the amino acid encodes at amino acid 670 other than lysine and/or at amino acid 671 other than methionine, and further encodes other than valine at amino acid 717, and where the host is an immortalized cell line.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-24,29 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 25-28,31 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated cells which comprise and express a nucleic

acid sequence encoding human amyloid precursor protein APP 770 operably linked to a promoter, wherein the amino acid encodes at amino acid 670 other than lysine and/or at amino acid 671 other than methionine, and further encodes other than valine at amino acid 717, such that detectable levels of said APP 770 are produced by the cells, and methods of screening using the cell lines, does not reasonably provide enablement for transgenic non-human mammals, hosts in the broadest definition by the specification and methods screening using the animals or hosts in their broadest definition by the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 21-32 are drawn to non-human transgenic animals containing in their germ or somatic cells a nucleic acid sequence encoding human amyloid precursor protein APP 770, wherein the amino acid encodes at amino acid 670 other than lysine and/or at amino acid 671 other than methionine, and further encodes other than valine at amino acid 717, wherein in the mouse exhibits neuropathological characteristics of Alzheimer's Disease, hosts containing a nucleic acid sequence encoding human amyloid precursor protein APP 770, wherein the amino acid encodes at amino acid 670 other than lysine and/or at amino acid 671 other than methionine, and further encodes other than valine at amino acid 717, and methods of screening agents capable of treating Alzheimer's disease comprising contacting an agent with the transgenic non-human animal and monitoring the expression, processing or deposition of amyloid precursor protein or fragments thereof.

For claims 21-32 enabled, the non-human transgenic animal host or the non-human transgenic animal must be readily available to the public from a reproducible source for animal, animal host or methods of screening to be enabled. However the specification does not provide either a source for the transgenic non-human animal or an enabling method of making the animal. The specification states that the transgene can be injected into mouse embryos and that the transgene can be identified to be integrated into the mouse genome.

However, applicant has not provided guidance as to which of the several constructs described on pages 23-25 will produce transgenic non-human animals or transgenic mice which express the integrated transgene to a level that the animals or the mouse can be used in a screening assay or otherwise as an Alzheimer's Disease model. For transgenic non-human animal, it was well established at the time of filing that not all transgenes will be expressed, although they may be integrated into the genome. Transgenic animals have within their cells cellular mechanisms which prevent expression of the transgene, such as DNA methylation or deletion from the genome (Kappell et al (1992) Current Opinion in Biotechnology 3, 549, col. 2, parag. 2). Applicant has not shown that the microinjection method reproducibly produces transgenic animals or mice which express the transgene so that the expression alters the phenotype of the animal or mouse such that it can serve as a model for Alzheimer's Disease, as disclosed in the specification (page 20, parag. 3). Evidence is not of record that the mice injected with one of applicant's disclosed transgenes will be expressed in the mouse such that the mouse develops a symptom or characteristic of Alzheimer's Disease. The art recognizes that certain brain pathologies are characteristic of Alzheimer's Disease. These include senile plaques, neurofibrillary tangles, neuritic processes and neuronal loss (Selkoe (1991) Nature 354, 432, col. 1, parag. 3, lines 1-20). Without a showing of a symptom(s) or characteristic(s) of Alzheimer's Disease, the mouse as disclosed would not have an enabled use as a AD model for use as a screening assay. The specification does not show such, and therefore the disclosed mice have not been shown to have neuropathological characteristics associated with Alzheimer's Disease. In addition, the art also taught that the production of transgenic mice expressing an APP transgene had been problematic, and that the reason was mice as a species may be resistant to the formation of Alzheimer's related pathologies and that sufficient expression of the APP transgene may be difficult to achieve (Lannfelt et al (1993) Behav. Brain Res. 57. page 210, col. 1, parag. 5; and col. 2, parag. 4, lines 8-16). In fact, transgenic mice which express the human APP-695 gene were known in the art not to

form amyloid protein deposits or neuritic processes (Higgins et al (1993) Annals NY Acad. Sci. 695, abstract). Also, at the time filing, the art taught that transgenic rats containing an APP transgene failed to demonstrate any Alzheimer's related pathology at six months of age (Felsenstein et al (1995) Alzheimer's and Parkinson's Diseases, I. Hanin, ed., Plenum Press, New York, page 406, page 1). These teachings indicate that the accessibility to the transgene would not predictably permit the artisan to produce a transgenic mouse that expresses the APP transgene to form neuropathological characteristics of Alzheimer's Disease. Thus the skilled artisan would be required to perform an undue amount of experimentation without a predictable degree of success in producing and using the transgenic mouse as disclosed.

It noted that in claims 21 and 23, it stated that the nucleic acid is contained within the animals germ or somatic cells. This is not enabled as the specification only teaches the production of transgenic non-human animals where the nucleic acid sequence is integrated into the genome and passes through the germ line to progeny. The specification does not enable chimeric non-human mammals where the nucleic acid is episomal or only in somatic cells. For the animal to be transgenic, the genome of the animals must comprise a nucleic acid. Further, the claims need to state that the nucleic acid is operably linked to a promoter as this is only means of expressing enabled by the specification.

As for the scope of isolated cells, the claims as written do not provide for an assay as there is no statement that the nucleic acid is operably linked to a promoter or that the APP 770 is produced to detectable levels. The specification only enables expression of nucleic acid sequence by a promoter and expression to a detectable level.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "immortalized cell line" in claims 25-28 is confusing as only mammalian cells are considered "immortal". The subject matter of "immortalized cell line" is not clear.

The term "capable of" in claims 29-32 is not clear as the specification does not disclose those factors that make the agents capable of or not capable of treating Alzheimer's Disease.

The word "promotes" in claims 29 and 30 does not clearly indicate the relationship between expression of the transgene and the development of Alzheimer's Disease neurological characteristics. A clearer word would be "results in".

The claims are free of the prior art. At the time of the instant invention, the prior art did not disclose or suggest a nucleic acid which encoded a human amyloid precursor protein where an amino acid other than lysine was at position 670 or an amino acid other than methionine was at position 671. Thus the prior art did not make or suggest a transgenic non-human animal or host which expressed this nucleic acid sequence, or a method of screening using either the transgenic non-human animal or the host.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (703) 308-1126.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Deborah Crouch

Dr. D. Crouch
April 16, 2002

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800/1630